

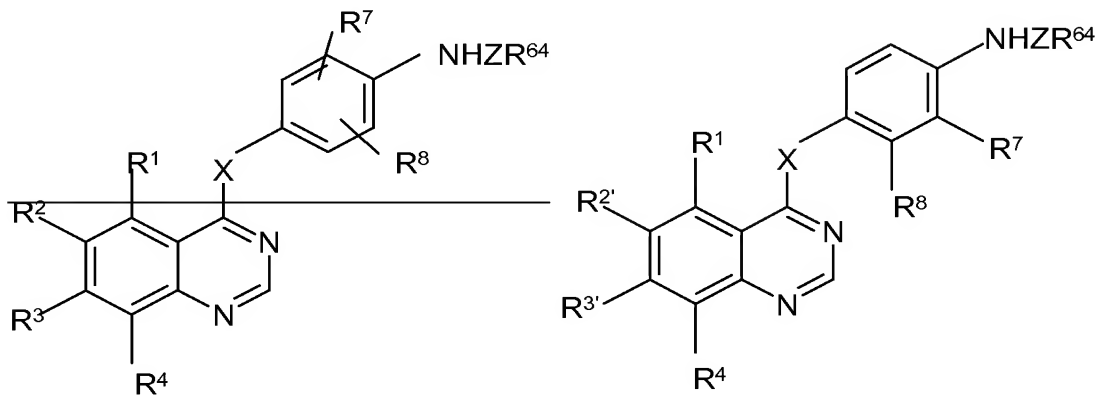
Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-19. (Cancelled)

20. (Currently amended) A compound of formula ~~(II C)~~ (II D)



or a salt, ~~ester or amide~~ thereof,

where X is NH;

Z is C(O);

R⁶⁴ is optionally substituted aryl selected from phenyl optionally substituted with up to 5 groups selected from nitro, halo, carboxy, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄alkylthio, acetoxy, acetamido, hydroxy, aminosulphonyl, C₁₋₄alkylsulphonyl, trifluoromethyl, arC₁₋₁₀alkyl, or arC₁₋₁₀alkyloxy wherein aryl rings in the substituents may themselves be substituted with halo, nitro or C₁₋₄alkyl; optionally substituted C₃₋₆cycloalkyl selected from optionally substituted cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl any of which may be optionally substituted with nitro, halo, carboxy, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄alkylthio, acetoxy, acetamido, hydroxy, aminosulphonyl, C₁₋₄alkylsulphonyl, trifluoromethyl, arC₁₋₁₀alkyl, arC₁₋₁₀alkyloxy, or aryl wherein aryl rings in the substituents may themselves be substituted with halo, nitro or C₁₋₄alkyl; optionally substituted arC₁₋₁₀alkyl selected from optionally substituted benzyl, phenylethyl or phenylpropyl, wherein the phenyl ring is optionally substituted with up to 5 groups selected from nitro, halo, carboxy, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄alkylthio, acetoxy, acetamido, hydroxy, aminosulphonyl, C₁₋₄alkylsulphonyl, trifluoromethyl, arC₁₋₁₀alkyl, or arC₁₋₁₀alkyloxy wherein aryl rings in the substituents may themselves be substituted with halo, carboxy, trifluoromethyl, nitro or C₁₋₄alkyl;

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optionally substituted heterocyclyl selected from pyridyl, pyrazine, pyrimidinyl, pyrrolidino, furyl, tetrahydrofuryl, oxazolyl, morpholino, thiadiazole, indolyl, quinolinyl, isoquinolinyl, pyrazolyl, methylenedioxybenzyl, thiophene and benzothiophene, all of which may be optionally substituted with one or more groups selected from nitro, halo, carboxy, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄alkylthio, acetoxyl, acetamido, hydroxy, aminosulphonyl, C₁₋₄alkylsulphonyl, trifluoromethyl, arC₁₋₁₀alkyl, or arC₁₋₁₀alkyloxy wherein aryl rings in the substituents may themselves be substituted with halo, carboxy, trifluoromethyl, nitro or C₁₋₄alkyl; optionally substituted C₁₋₁₀alkyl where optional substituents for C₁₋₁₀alkyl include amino, mono- or di-C₁₋₄alkylamino, hydroxy, C₁₋₄alkoxy, heterocyclyl selected from thiophene, tetrahydrothiophene-1,1-dioxide, pyrrolidino, morpholino, furyl and tetrahydrofuryl, C₁₋₄alkoxy, acetamido, aryloxy, alkylC₁₋₄thio, aroyl where the aryl ring may itself be substituted with halo, carboxy, trifluoromethyl, nitro, carboxy or trifluoromethyl, C₃₋₁₀cycloalkyl or C₃₋₁₀cycloalkenyl; or optionally substituted C₂₋₁₀alkenyl or C₂₋₁₀alkynyl where optional substituents for C₂₋₁₀alkenyl or C₂₋₁₀alkynyl include nitro, halo, carboxy, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄alkylthio, acetoxyl, acetamido, hydroxy, aminosulphonyl, C₁₋₄alkylsulphonyl, trifluoromethyl, arC₁₋₁₀alkyl, or arC₁₋₁₀alkyloxy wherein aryl rings in the substituents may themselves be substituted with halo, carboxy, trifluoromethyl, nitro or C₁₋₄alkyl; or such groups are substituted by aryl, where the aryl ring may itself be substituted with halo, nitro, carboxy, trifluoromethyl; R⁷ and R⁸ are independently selected from hydrogen, halo, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄alkoxymethyl, di(C₁₋₄alkoxy)methyl, C₁₋₄alkanoyl, trifluoromethyl, cyano, amino, C₂₋₅alkenyl, C₂₋₅alkynyl, a phenyl group, a benzyl group or a 5-6-membered heterocyclic group with 1-3 heteroatoms, selected independently from O, S and N, which heterocyclic group may be aromatic or non-aromatic and may be saturated, and linked via a ring carbon or nitrogen atom, or unsaturated, and linked via a ring carbon atom, and which phenyl, benzyl or heterocyclic group may bear on one or more ring carbon atoms up to 5 substituents selected from hydroxy, halogeno, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃alkanoyloxy, trifluoromethyl, cyano, amino, nitro, C₂₋₄alkanoyl, C₁₋₄alkanoylamino, C₁₋₄alkoxycarbonyl, C₁₋₄alkylsulphanyl, C₁₋₄alkylsulphinyl, C₁₋₄alkylsulphonyl, carbamoyl, N-C₁₋₄alkylcarbamoyl, N,N-di(C₁₋₄alkyl)carbamoyl, aminosulphonyl, N-C₁₋₄alkylaminosulphonyl, N,N-di(C₁₋₄alkyl)aminosulphonyl, C₁₋₄alkylsulphonylamino, and a saturated heterocyclic group selected from morpholino, thiomorpholino, pyrrolidinyl, piperazinyl, piperidinyl, imidazolidinyl and pyrazolidinyl, which saturated heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃alkanoyloxy, trifluoromethyl, cyano, amino, nitro and C₁₋₄alkoxycarbonyl, and

where R^1 , R^2 , R^3 and R^4 are independently selected from halo, cyano, nitro, or $-X^1R^{15}$, wherein X^1 represents a direct bond, $-O-$, $-CH_2-$, $-OCO-$, carbonyl, $-S-$, $-SO-$, $-SO_2-$, $-NR^{16}CO-$, $-CONR^{16}-$, $-SO_2NR^{16}-$, $-NR^{17}SO_2-$ or $-NR^{18}-$, wherein R^{16} , R^{17} and R^{18} each independently represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl, and R^{15} is selected from one of the following groups:

- 1') hydrogen or C_{1-5} alkyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, fluoro or amino;
- 2') $C_{1-5}alkylX^2COR^{19}$ wherein X^2 represents $-O-$ or $-NR^{20}-$, in which R^{20} represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl, and R^{19} represents C_{1-3} alkyl, $-NR^{21}R^{22}$ or $-OR^{23}$, wherein R^{21} , R^{22} and R^{23} which may be the same or different each represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl;
- 3') $C_{1-5}alkylX^3R^{24}$ wherein X^3 represents $-O-$, $-S-$, $-SO-$, $-SO_2-$, $-OCO-$, $-NR^{25}CO-$, $-CONR^{26}-$, $-SO_2NR^{27}-$, $-NR^{28}SO_2-$ or $-NR^{29}-$, wherein R^{25} , R^{26} , R^{27} , R^{28} and R^{29} each independently represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl, and R^{24} represents hydrogen, C_{1-3} alkyl, cyclopentyl, cyclohexyl or a 5-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C_{1-3} alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and C_{1-4} alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-4} alkyl, C_{1-4} hydroxyalkyl and C_{1-4} alkoxy;
- 4') $C_{1-5}alkylX^4C_{1-5}alkylX^5R^{30}$ wherein X^4 and X^5 which may be the same or different are each $-O-$, $-S-$, $-SO-$, $-SO_2-$, $-NR^{31}CO-$, $-CONR^{32}-$, $-SO_2NR^{33}-$, $-NR^{34}SO_2-$ or $-NR^{35}-$, wherein R^{31} , R^{32} , R^{33} , R^{34} and R^{35} each independently represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl, and R^{30} represents hydrogen or C_{1-3} alkyl;
- 5') R^{36} wherein R^{36} is a 5-6-membered saturated heterocyclic group, linked via carbon or nitrogen, with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-4} alkyl, C_{1-4} hydroxyalkyl, C_{1-4} alkoxy, C_{1-4} alkoxy C_{1-4} alkyl and $C_{1-4}alkylsulphonylC_{1-4}alkyl$;
- 6') $C_{1-5}alkylR^{36}$ wherein R^{36} is as defined in (5') above;
- 7') $C_{2-5}alkenylR^{36}$ wherein R^{36} is as defined in (5') above;
- 8') $C_{2-5}alkynylR^{36}$ wherein R^{36} is as defined in (5') above;
- 9') R^{37} wherein R^{37} represents a pyridone group, a phenyl group or a 5-6-membered aromatic heterocyclic group, linked via carbon or nitrogen, with 1-3 heteroatoms selected from O, N and S, which pyridone, phenyl or aromatic heterocyclic group may carry up to 5 substituents on an available carbon atom selected from hydroxy, halogeno, amino, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} hydroxyalkyl, C_{1-4} aminoalkyl, $C_{1-4}alkylamino$, $C_{1-4}hydroxyalkoxy$, carboxy, trifluoromethyl,

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cyano, $-\text{CONR}^{38}\text{R}^{39}$ and $-\text{NR}^{40}\text{COR}^{41}$, wherein R^{38} , R^{39} , R^{40} and R^{41} , which may be the same or different, each represents hydrogen, C_{1-4} alkyl or C_{1-3} alkoxy C_{2-3} alkyl;

10') C_{1-5} alkyl R^{37} wherein R^{37} is as defined in (9') above;

11') C_{2-5} alkenyl R^{37} wherein R^{37} is as defined in (9') above;

12') C_{2-5} alkynyl R^{37} wherein R^{37} is as defined in (9') above;

13') C_{1-5} alkyl X^6R^{37} wherein X^6 represents $-\text{O}-$, $-\text{S}-$, $-\text{SO}-$, $-\text{SO}_2-$, $-\text{NR}^{42}\text{CO}-$, $-\text{CONR}^{43}-$, $-\text{SO}_2\text{NR}^{44}-$, $-\text{NR}^{45}\text{SO}_2-$ or $-\text{NR}^{46}-$, wherein R^{42} , R^{43} , R^{44} , R^{45} and R^{46} each independently represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl, and R^{37} is as defined hereinbefore;

14') C_{2-5} alkenyl X^7R^{37} wherein X^7 represents $-\text{O}-$, $-\text{S}-$, $-\text{SO}-$, $-\text{SO}_2-$, $-\text{NR}^{47}\text{CO}-$, $-\text{CONR}^{48}-$, $-\text{SO}_2\text{NR}^{49}-$, $-\text{NR}^{50}\text{SO}_2-$ or $-\text{NR}^{51}-$, wherein R^{47} , R^{48} , R^{49} , R^{50} and R^{51} each independently represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl, and R^{37} is as defined in (9') above;

15') C_{2-5} alkynyl X^8R^{37} wherein X^8 represents $-\text{O}-$, $-\text{S}-$, $-\text{SO}-$, $-\text{SO}_2-$, $-\text{NR}^{52}\text{CO}-$, $-\text{CONR}^{53}-$, $-\text{SO}_2\text{NR}^{54}-$, $-\text{NR}^{55}\text{SO}_2-$ or $-\text{NR}^{56}-$, wherein R^{52} , R^{53} , R^{54} , R^{55} and R^{56} each independently represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl, and R^{37} is as defined hereinbefore;

16') C_{1-3} alkyl X^9C_{1-3} alkyl R^{37} wherein X^9 represents $-\text{O}-$, $-\text{S}-$, $-\text{SO}-$, $-\text{SO}_2-$, $-\text{NR}^{57}\text{CO}-$, $-\text{CONR}^{58}-$, $-\text{SO}_2\text{NR}^{59}-$, $-\text{NR}^{60}\text{SO}_2-$ or $-\text{NR}^{61}-$, wherein R^{57} , R^{58} , R^{59} , R^{60} and R^{61} each independently represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl, and R^{37} is as defined hereinbefore; and

17') C_{1-3} alkyl X^9C_{1-3} alkyl R^{36} wherein X^9 and R^{36} are as defined in (5') above;

and R^{37} is a group $\text{X}^1-\text{R}^{15'}$ and $\text{X}^{15'}$ is as defined for R^{15} provided that it is other than methyl.

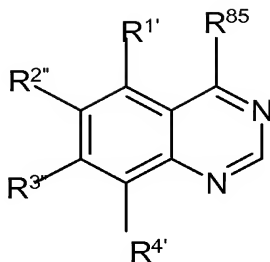
~~provided that i) where R^1 , R^4 , R^7 and R^8 are all hydrogen and R^2 and R^3 are both hydrogen or both methoxy, R^{64} is other than phenyl;~~

~~(ii) where R^1 , R^4 , R^7 and R^8 are all hydrogen and R^2 and R^3 are methoxy, R^{64} is other than methyl; and~~

~~iii) wherein at least one of R^1 or R^4 is $-\text{X}^4\text{R}^{15'}$.~~

21-26. (Cancelled)

27. (Currently amended) A method for preparing a compound according to claim 20, which method comprises reacting a compound of formula (VIII)



(VIII)

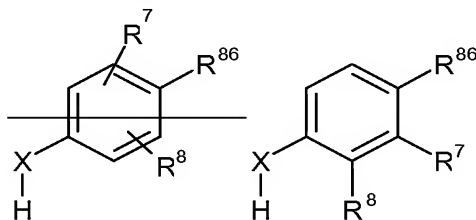
where R^{1'} is equivalent to the corresponding group of formula R¹ as defined in relation to the said compound of claim 20, or a precursor thereof;

R^{2''} is equivalent to the corresponding group of formula R² as defined in relation to the said compound of claim 20, or a precursor thereof;

R^{3''} is equivalent to the corresponding group of formula R³ as defined in relation to the said compound of claim 20, or a precursor thereof;

R^{4'} is equivalent to the corresponding group of formula R⁴ as defined in relation to the said compound of claim 20, or a precursor thereof;

and R⁸⁵ is a leaving group, with a compound of formula (IX')



(IX')

where X, R⁷ and R⁸ are as defined in relation to the said compound according to claim 20, and R⁸⁶ is a group of formula NHZR⁶⁴ where Z and R⁶⁴ as are defined in relation to the said compound in claim 20; and thereafter if desired or necessary converting a group ~~R^{1'}, R^{2''}, R^{3''} or R^{4'} to a group R¹, R², R³ or R⁴ respectively or to a different such group.~~

28-29. (Cancelled)

30. (Currently amended) A pharmaceutical composition comprising a compound of formula ~~(IIC)~~(IID) as defined in claim 20, or a pharmaceutically acceptable salt ~~or an *in vivo* hydrolysable ester, or amide~~ thereof, in combination with a pharmaceutically acceptable carrier.

31-33. (Cancelled)

34. (Previously presented) A compound according to claim 20, wherein R⁶⁴ is phenyl, 2-furan, (E)-CH=CH-phenyl, 3,4,5-trimethoxyphenyl, 2,4-difluorophenyl, 2-nitro-4,5-dimethoxyphenyl, 2,4-dinitrophenyl, 2-fluorobenzyl, cyclopentyl, 1-methylbut-3-enyl, n-heptyl, 2-(methylthio)ethyl, 2-ethoxyethyl, C(CH₃)=CH₂, 5-methyl-2-pyrazine, 3-furyl, 3-cyanophenyl, 4-acetoxyphenyl, 2-nitro-3-methoxyphenyl, 2-methylthiophenyl, 3-acetoxyphenyl, 2-pyridyl, 2-quinoliny, 1,5-dimethyl-1H-pyrazolyl, 2-fluoro-5-nitrophenyl, 3-pyridyl, 2-chloro-3-pyridyl, 2-fluorophenyl, 2,3-difluorophenyl, 2,5-difluorophenyl, 2,3-dimethoxyphenyl, 3,5-dimethoxy-4-hydroxy-phenyl, 3-chloro-4-carboxyphenyl, 3-nitro-4-(methylsulphonyl)-phenyl, 3-nitro-4-methoxyphenyl, (E)-CH=CH-(2-nitrophenyl), (E)-CH=CH-(3-nitrophenyl), (E)-CH=CH-(4-nitrophenyl), (E)-CH=CH-(4-chlorophenyl), (E)-CH=CH-(2,3,4-trifluoro-phenyl), (E)-CH=CH-(3-(trifluoromethyl)phenyl), (E)-CH=CH-(4-fluorophenyl), 2-indolyl, 5-fluoro-2-indolyl, 3-fluorophenyl, 3,5-dinitrophenyl, 3-(trifluoromethyl)benzyl, 3-fluorobenzyl, 4-chlorobenzyl, 4-methoxybenzyl, 4-(*iso*-propyl)benzyl, 3-nitrobenzyl, 2-phenoxyethyl, 2-(3,4-dimethoxyphenyl)ethyl, 2-(4-chlorobenzoyl)ethyl, 3-phenoxy-1-propyl, 3-phenyl-1-propyl, 3-benzoylpropyl, dec-9-enyl, 1-methylbut-1-enyl, (2-thiophene)methyl, (3-thiophene)methyl, 2-(3-nitro-4-hydroxyphenyl)ethyl, 3,5-difluorobenzyl, 3,4-methylenedioxybenzyl, 2,6-difluorobenzyl, 4-(n-butoxy)benzyl, 3-methyl-1-butyl, pent-4-ynyl, 3-(5-bromo-4-methoxy)thiophene, 3-(5-chloro-4-methoxy)-thiophene, 3-methoxy-4-ethoxybenzyl, 4-(benzyloxy)benzyl, 3-(2-thiophene)propyl, hex-5-ynyl, 1-(4-chlorophenyl)cyclopropyl, cyclopentylmethyl, 2-(cyclopentyl)ethyl, cyclohexylmethyl, 2-(cyclohexyl)ethyl, 3-(cyclohexyl)propyl, 1-phenoxyethyl, (E)-C(CH₃)=CH-phenyl, 2-chloro-5-nitrophenyl, methyl, n-heptyl, 2-furyl, 3-furyl, (2-thiophene)methyl, 2-indolyl, 2,4-difluorophenyl, (3-nitro-4-(methylsulphonyl))-phenyl, pent-4-ynyl, 5-methyl-2-pyrazinyl, cyclopentyl, 3-nitro-4-methoxyphenyl, 2-tetrahydrofuryl, 2-pyridyl, 3-pyridyl, 1,5-dimethyl-pyrazol-3-yl, cyclobutyl, 2-methoxyphenyl, 3-nitrophenyl, 4-nitrophenyl, cyclohexyl, 3-nitro-4-methylphenyl, 3-nitro-4-fluorophenyl, (3-thiophene)methyl, 3-chloro-2-benzothiophene, 5-chloro-2-indolyl, but-3-ynyl, 3-cyanophenyl, 2-(acetamido)ethyl, 4-(trifluoromethyl)phenyl, 3-chloro-4-fluorophenyl, 4-fluoro-3-(trifluoromethyl)-phenyl, 4-fluorophenyl, 5-bromo-2-thiophene, 4-methoxyphenyl, 6-methyl-3-pyridyl, 5-nitro-2-furyl, 2-nitrophenyl, (E)-CH=CH-(3-chlorophenyl), 2-thiophene, cyclopropyl, 3-methylphenyl, 2-chlorophenyl, 2-fluorophenyl, 2,5-dichlorophenyl, 3-fluorophenyl, 6-chloro-3-pyridyl, 5-bromo-2-furyl, 3-nitro-2-methylphenyl, 3-chlorophenyl, 3-(tetrahydrothiophene-1-1'-dioxide)methyl, 2-methoxyethyl or 2-(methylthio)phenyl.

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35. (Previously presented) A compound according to claim 20, where R⁶⁴ is phenyl or halosubstituted phenyl.

36. (Previously presented) A compound according to claim 20, where R¹ is hydrogen and R⁴ is halo, C₁₋₄alkyl or C₁₋₄alkoxy.

37. (Previously presented) A compound according to claim 20, where X¹ is oxygen.

38. (Previously presented) A compound according to claim 20, where R¹⁵ is selected from a group (1'), (3'), (6') or (10') as defined in claim 20.

39. (Previously presented) A compound according to claim 20, where R⁷ and R⁸ are independently selected from hydrogen, halo, C₁₋₄alkoxy, cyano, trifluoromethyl or phenyl.

40. (Cancelled)

41. (Previously presented) A compound according to claim 20 where R¹ is hydrogen, R⁴ is halo, C₁₋₄alkyl or C₁₋₄alkoxy, X¹ is oxygen, R¹⁵ is selected from a group (1'), (3'), (6') or (10') as defined in claim 20 and R⁷ and R⁸ are independently selected from hydrogen, halo, C₁₋₄alkoxy, cyano, trifluoromethyl or phenyl.

42. (Previously presented) A compound according to claim 41 where R⁶⁴ is phenyl or halosubstituted phenyl.

43. (Previously presented) A compound according to claim 34 wherein R¹ is hydrogen, R⁴ is halo, C₁₋₄alkyl or C₁₋₄alkoxy, X¹ is oxygen, R¹⁵ is selected from a group (1'), (3'), (6') or (10') as defined in claim 20 and R⁷ and R⁸ are independently selected from hydrogen, halo, C₁₋₄alkoxy, cyano, trifluoromethyl or phenyl.

44. (Currently amended) A method of treating colorectal or breast cancer in a warm blooded animal in need of such treatment, which comprises administering to said animal an effective amount of a compound of formula ~~(I)~~(IID), as claimed in claim 20.